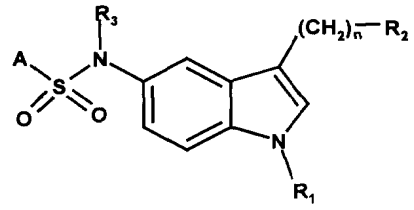
SULPHONAMIDE DERIVATIVES, THEIR PREPARATION AND USE AS MEDICAMENTS

Field of the Invention

The present invention relates to new sulphonamide derivatives, with the general formula (I), as well as to their physiologically acceptable salts, the processes for their preparation, their application as medicaments in human and/or veterinary therapy and the pharmaceutical compositions that contain them.



(I)

The new compounds object of the present invention can be used in the pharmaceutical industry as intermediates and for preparing medicaments.

Background of the invention

The superfamily of serotonin receptors (5-HT) includes 7 classes (5-HT_1-5-HT_7) encompassing 14 human subclasses [D. Hoyer, et al., *Neuropharmacology*, **1997**, *36*, 419]. The 5-HT_6 receptor is the latest serotonin receptor identified by molecular cloning both in rats [F.J. Monsma, et al., *Mol. Pharmacol.*, **1993**, *43*, 320; M. Ruat, et al., *Biochem. Biophys. Res. Commun.*, **1993**, *193*, 268] and in humans [R. Kohen, et al., *J. Neurochem.*, **1996**, *66*, 47]. Compounds with 5-HT_6 receptor antagonistic activity are useful for the treatment of various disorders of the Central Nervous System and of the gastrointestinal tract, such as irritable bowel syndrome. Compounds with 5-HT_6 receptor antagonistic activity are useful in the treatment of anxiety, depression and cognitive memory disorders [M. Yoshioka, et al., *Ann. NY Acad. Sci.*, **1998**, *861*, 244; A. Bourson, et al., *Br. J. Pharmacol.* , **1998**, *125*, 1562; D.C. Rogers, et al., *Br. J. Pharmacol. Suppl.*, **1999**, *127*, 22P; A. Bourson, et al., *J. Pharmacol. Exp. Ther.* , **1995**, *274*, 173; A.J. Sleight, et al., *Behav. Brain Res.* ,

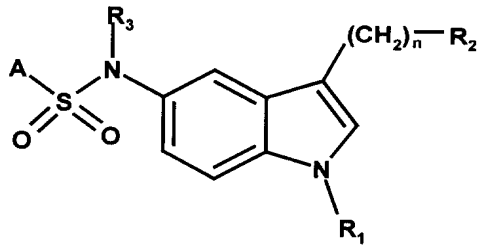
1996, *73*, 245; T.A. Branchek, et al., *Annu. Rev. Pharmacol. Toxicol.* , **2000**, *40*, 319; C. Routledge, et al., *Br. J. Pharmacol.* , **2000**, *130*, 1606]. It has been shown that typical and atypical antipsychotic drugs for treating schizophrenia have a high affinity for 5-HT_6 receptors [B.L. Roth, et al., *J. Pharmacol. Exp. Ther.* , **1994**, *268*, 1403; C.E. Glatt, et al., *Mol. Med.* , **1995**, *1*, 398; F.J. Mosma, et al., *Mol. Pharmacol.* , **1993**, *43*, 320; T. Shinkai, et al., *Am. J. Med. Genet.* , **1999**, *88*, 120]. Compounds with 5-HT_6 receptor antagonistic activity are useful for treating infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) [W.D. Hirst, et al., *Br. J. Pharmacol.* , **2000**, *130*, 1597; C. Gérard, et al., *Brain Research* , **1997**, *746*, 207; M.R. Pranzatelli, *Drugs of Today* , **1997**, *33*, 379]. Patent application WO 01/32646 describes sulphonamides derived from bicycles, with 6 members each, aromatic or heteroaromatic with 5-HT_6 receptor antagonistic activity. Patent application EP 0733628 describes sulphonamides derived from indole with an 5-HT_{1F} receptor antagonistic activity useful for treating migraines. In general, the study of the scientific literature and patents indicates that small structural variations give rise to agonist or antagonist compounds of various receptors of serotonin that are useful for treating different diseases, depending on the receptor for which they show affinity.

After laborious research the inventors have managed to synthesize new compounds with the general formula (I) that show interesting biological properties making them particularly useful for use in human and/or veterinary therapy.

Detailed description of the invention

The present invention provides new compounds with serotonin 5-HT6 receptor antagonistic activity useful in the preparation of a medicament for prevention or treatment of various disorders of the Central Nervous System, and in particular anxiety, depression, cognitive memory disorders and senile dementia or other dementia processes in which there is a predominant cognition deficit, psychosis, infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the serotonin 5-HT_6 receptor in mammals, including man.

The compounds object of the present invention have the general formula (I)

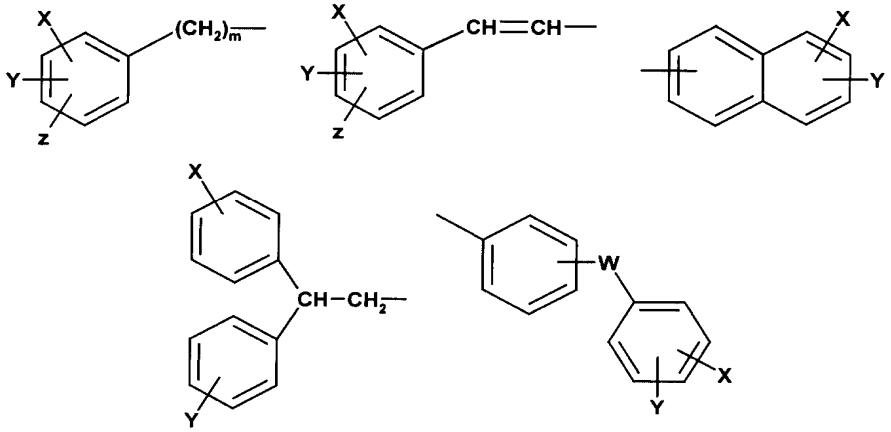


(I)

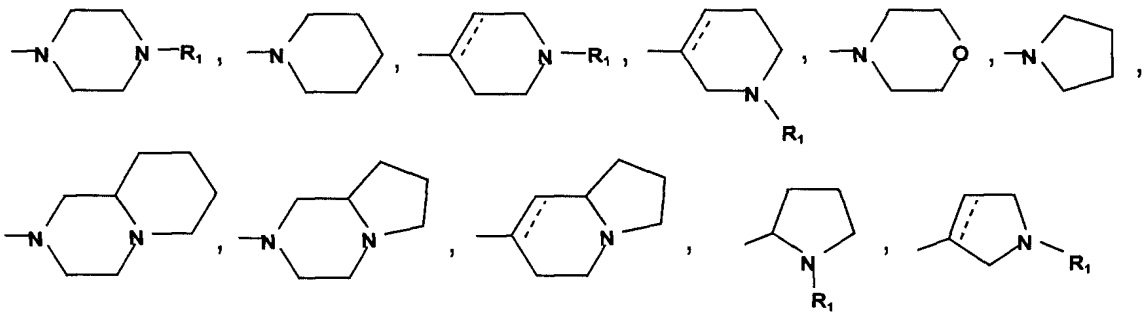
wherein

A represents a substituent selected from among:

- a heteroaromatic ring of 5 or 6 members containing 1 or 2 heteroatoms selected from among oxygen, nitrogen and sulphur, optionally substituted by 1 or 2 halogen atoms, by a C_1-C_4 alkyl radical or by a phenyl radical or a heteroaryl radical with 5 or 6 members containing 1 or 2 atoms of oxygen, nitrogen or sulphur;
- a bicyclic heteroaromatic ring containing 1 to 3 heteroatoms selected from among oxygen, nitrogen and sulphur, optionally substituted by 1 or 2 halogen atoms or by a C_1-C_4 alkyl radical;
- a group selected from among:



R_1 represents hydrogen, a C_1-C_4 alkyl radical or a benzyl radical;
n represents 0, 1, 2, 3 or 4;
R_2 represents $-NR_4R_5$ or a group with formula:



wherein the dotted line represents an optional chemical bond;

R_3, R_4 y **R_5** independently represent hydrogen or a C_1-C_4 alkyl;
X, Y and **Z** independently represent hydrogen, fluorine, chlorine, bromine, a C_1-C_4 alkyl, a C_1-C_4 alkoxy, a C_1-C_4 alkylthio, trifluoromethyl, cyano, nitro and $-NR_4R_5$;
W represents a bond between the two rings, CH_2, O, S and NR_4;
m represents 0, 1, 2, 3 or 4;
with the proviso that when **m** = 0, **A** is a substituted phenyl;
or one of its physiologically acceptable salts.

The alkyl term C_1-C_4 represents a linear or branched hydrocarbon chain including 1 to 4 atoms of carbon, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl and *tert-but*yl.

Compounds object of the present invention that correspond to the above formula can be selected from among:

[1] N-[3-(2-diethylaminoethyl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.
[2] N-[3-(2-diethylaminoethyl)-1H-indol-5-yl]naphthalene-1-sulphonamide.
[3] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide hydrochloride.
[4] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-3,5-dichlorobenzenesulphonamide.
[5] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-4-phenylbenzenesulphonamide.
[6] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-5-chlorothiophene-2-sulphonamide.

[7] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.

[8] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide.

[9] N-[3-(2-dimethylamino-ethyl)-1*H*-indol-5-yl]-6-chloroimidazo[2,1-b]thiazol-5-sulphonamide.

[10] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.

[11] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide hydrochloride.

[12] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide.

[13] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide hydrochloride.

[14] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]-5-chlorothiophene-2-sulphonamide.

[15] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]-4-phenylbenzenesulphonamide.

[16] N-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]quinoline-8-sulphonamide.

[17] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]naphthalene-2-sulphonamide.

[18] N-[3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide.

[19] N-[3-(4-methylpiperazin-1-yl)methyl-1*H*-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.

[20] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-5-(2-pyridil)thiophene-2-sulphonamide.

[21] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-2,1,3- benzothiadiazol-4-sulphonamide.

[22] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]quinoline-8-sulphonamide.

[23] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-5-chloronaphthalene-2-sulphonamide.

[24] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-4-phenoxybenzenesulphonamide.

[25] N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-4-phenylbenzenesulphonamide.

[26] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-N-ethyl-naphthalene-2-sulphonamide.

[27] N-{3-[2-(morpholin-4-yl)ethyl]-1H-indol-5-yl}-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.

[28] N-{3-[2-(morpholin-4-yl)ethyl]-1H-indol-5-yl}naphthalene-1-sulphonamide.

[29] N-[3-(2-diethylaminoethyl)-1H-indol-5-yl]naphthalene-2-sulphonamide.

[30] N-[3-dimethylaminomethyl-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.

[31] N-[3-(2-dipropylaminoethyl)-1H-indol-5-yl]naphthalene-1-sulphonamide.

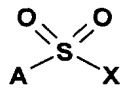
[32] N-[3-(2-dipropylaminoethyl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.
[33] N-[3-(2-dibutylaminoethyl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.
[34] N-[3-(2-dibutylaminoethyl)-1H-indol-5-yl]naphthalene-1-sulphonamide.
[35] N-[3-(2-diethylaminoethyl)-1H-indol-5-yl]-5-chloronaphthalene-1-sulphonamide.
[36] N-[3-(2-diethylaminoethyl)-1H-indol-5-yl]-trans-β-styrenesulphonamide.
[37] N-[3-(4-methylpiperazin-1-yl)methyl-1*H*-indol-5-yl]-trans-β-styrenesulphonamide.
[38] N-[3-(octahydroindolizin-7-yl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.
[39] N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-6-chloroimidazo[2,1-b]thiazol-5-sulphonamide.
[40] N-{3-[2-(morpholin-4-yl)ethyl]-1H-indol-5-yl}naphthalene-2-sulphonamide.
[41] N-[3-(4-methylpiperazin-1-yl)methyl-1*H*-indol-5-yl]-α-toluenesulphonamide.
[42] N-[3-(3-diethylaminopropyl)-1H-indol-5-yl]naphthalene-2-sulphonamide.
[43] N-[3-(3-diethylaminopropyl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.
[44] N-{3-[2-(pyrrolidin-1-yl)ethyl]-1H-indol-5-yl}-5-chloro-3-methylbenzo[b]thiophene-2-sulphonamide.
[45] N-{3-[2-(pyrrolidin-1-yl)ethyl]-1H-indol-5-yl}naphthalene-1-sulphonamide.
[46] N-{3-[2-(pyrrolidin-1-yl)ethyl]-1H-indol-5-yl}naphthalene-2-sulphonamide.
[47] N-[3-(2-dipropylaminoethyl)-1H-indol-5-yl]naphthalene-2-sulphonamide.
[48] N-[3-(2-dimethylaminoethyl)-1H-indol-5-yl]-5-chloronaphthalene-1-sulphonamide.
[49] N-[3-(2-dimethylaminoethyl)-1H-indol-5-yl]naphthalene-2-sulphonamide.
[50] N-{3-[2-(morpholin-4-yl)ethyl]-1H-indol-5-yl}quinoline-8-sulphonamide.
[51] N-{3-[2-(morpholin-4-yl)ethyl]-1H-indol-5-yl}-4-phenylbenzenesulphonamide.
[52] N-[3-(4-methylpiperazin-1-yl)ethyl-1*H*-indol-5-yl]naphthalene-2-sulphonamide.
[53] N-[3-(4-methylpiperazin-1-yl)ethyl-1*H*-indol-5-yl]-5-chloronaphthalene-1-sulphonamide.

The present invention also relates to the physiologically acceptable salts of the compounds with the general formula (I), particularly the addition salts of mineral acids such as hydrochloric, hydrobromic, phosphoric, sulphuric, nitric acids, and of organic acids such as citric, maleic, fumaric, tartaric acids or their derivatives, *p*-toluensulphonic acid, methansulphonic acid, camphorsulphonic acid, etc.

The new derivatives with the general formula (I), wherein R_1, R_2, R_3, R_4, n and A have the meanings indicated above, can be prepared according to the following methods:

METHOD A

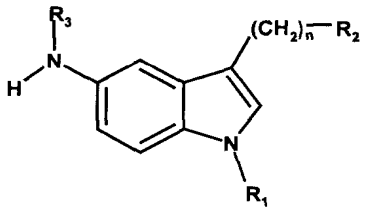
By reacting a compound with the general formula (II) or one of its suitably protected derivatives



(II)

wherein A has the meaning indicated previously in the general formula (I) and X is an acceptable leaving group including a halogen atom, particularly chlorine;

with a 5-aminoindole with the general formula (III), or one of its suitably protected derivatives;



(III)

wherein n, R_1, R_2 and R_3 have the meanings indicated previously in the general formula (I);
in order to obtain the corresponding sulphonamide and, optionally, removing from it the protective groups and / or forming a pharmacologically acceptable salt.

The reaction between the compounds with the general formula (II) and (III) is carried out in the presence of an organic solvent such as an alkyl ether, particularly diethyl ether, or a cycloalkyl ether, particularly tetrahydrofurane or dioxane, a halogenated organic hydrocarbon, particularly methylene chloride or

chloroform, an alcohol, particularly methanol or ethanol, an aprotic dipolar solvent, particularly acetonitrile, pyridine or dimethylformamide, or any other suitable solvent.

The reaction preferably is carried out in the presence of a suitable inorganic base such as hydroxides and carbonates of alkali metals, or in the presence of an organic base, particularly triethylamine or pyridine.

The most suitable reaction temperatures range from 0 ° C to room temperature, and the reaction time is between 5 minutes and 24 hours.

The resulting sulphonamide can be isolated by evaporating the solvent, adding water and eventually adjusting the pH so that it is obtained as a solid that can be isolated by filtration; or it can be extracted by a solvent immiscible with water such as chloroform and purified by chromatography or recrystallisation from a suitable solvent.

The compounds with the general formula (II) are commercially available or can be prepared according to standard methods or by methods analogous to those described in the literature [E.E. Gilbert, *Synthesis*, **1969**, *1*, 3] and the compounds with the general formula (III) can be prepared according to standard methods or by methods analogous to those described in the literature [J.E. Macor, R. Post and K. Ryan, *Synt Comm.*, **1993**, *23*, 1, 65-72.; J. Guillaume, C. Dumont, J. Laurent and N. Nédélec, *Eur. J. Med. Chem.*, **1987**, *22*, 33-43; M.L. Saccarello, R. Stradi, *Synthesis*, **1979**, 727].

METHOD B

The compounds with the general formula (I), wherein R_1, R_2, R_4, n and A have the meanings indicated above and R_3 represents a C_1-C_4 alkyl, can be prepared by alkylation of a compound with the general formula (I), wherein R_1, R_2, R_4, n and A have the meanings indicated above and R_3 represents an atom of hydrogen, with an alkyl halide or a dialkyl sulphate.

The reaction preferably is carried out in the presence of a suitable base such as hydroxides and carbonates of alkali metals, metal hydrides, alkoxides such as sodium methoxide or potassium tert-butoxide, organometallic compounds such as butyl lithium or tert-butyl lithium, in the presence of an organic solvent such as an alkyl ether, particularly diethyl ether, or a cycloalkyl ether, particularly

tetrahydrofurane or dioxane, a hydrocarbon, particularly toluene, an alcohol, particularly methanol or ethanol, an aprotic dipolar solvent, particularly acetonitrile, pyridine or dimethylformamide, or any other suitable solvent. The most suitable temperatures are between 0 ° C and the boiling point of the solvent, and reaction times are between 1 and 24 hours.

The resulting sulphonamide can be isolated by concentrating the filtrate at reduced pressure, adding water and eventually adjusting the pH so that it is obtained as a solid that can be isolated by filtration, or it can be extracted with a solvent immiscible with water such as chloroform and purified by chromatography or recrystallisation from a suitable solvent.

METHOD C

By condensation of a compound with the general formula (I) wherein R_1, R_3, and A have the meanings indicated above, n=0 and R_2 represents an atom of hydrogen, with a suitably substituted 4-piperidone the corresponding compound is obtained with the general formula (I) wherein R_1, R_3, and A have the meanings indicated above, n=0 and R_2 represents a suitably substituted 1,2,3,6-tetrahydropyridine-4-yl radical.

The reaction can take place in both an acid and a basic medium, in a suitable solvent at temperatures between 25 and 150° C.

Suitable basic conditions include inorganic bases such as sodium or potassium hydroxide, or organic bases such as pyrrolidine or triethylamine in solvents such as methanol or ethanol. Preferably, solutions of sodium methoxide in methanol at reflux. Reaction times range from 1 to 48 hours.

Suitable acidic conditions include hydrochloric acid in ethanol or trifluoroacetic acid in acetic acid at temperatures between 50 and 100° C and reaction times ranging from 1 to 48 hours.

The resulting sulphonamide can be isolated by dilution in water, eventually adjusting the pH, to obtain it as a solid that can be isolated by filtration; or it can be extracted with a solvent immiscible with water such as chloroform and purified by chromatography or by recrystallisation from a suitable solvent.

The compounds with the general formula (I) wherein R_1, R_3, and A have the meanings indicated above, n=0 and R_2 represents an atom of hydrogen, can be prepared according to the method A from a 5-aminoindole.

METHOD D

The compounds with the general formula (I) wherein R_1, R_3, and A have the meanings indicated above, n=0 and R_2 represents a suitably substituted 4-piperidinyl radical, can be prepared by reducing a compound with the general formula (I) wherein R_1, R_3, and A have the meanings indicated above, n=0 and R_2 represents a suitably substituted 1,2,3,6-tetrahydropyridin-4-yl radical prepared according to the method C.

Hydrogenation takes place with the aid of a metallic catalyst such as palladium, platinum or rhodium on a support such as carbon, aluminum oxide or barium sulphate, preferably palladium over carbon, with an initial hydrogen pressure of between 1 and 10 atmospheres, preferably between 2 and 5 atmospheres, in a solvent such as methanol or ethanol. The reaction time ranges from 1 hour to 3 days.

The resulting sulphonamide can be isolated by filtering the catalyst and concentrating the filtrate at reduced pressure. The product recovered can be used as such or it can be purified by chromatography or by recrystallisation from a suitable solvent.

METHOD E

The pharmacologically acceptable salts of compounds with the general formula (I) can be conventionally prepared by reaction with a mineral acid, such as hydrochloric, hydrobromic, phosphoric, sulphuric, nitric acids or with organic acids such as citric, maleic, fumaric, tartaric acids or their derivatives, *p*-toluensulphonic acid, methansulphonic acid, etc., in a suitable solvent such as methanol, ethanol, ethyl ether, ethyl acetate, acetonitrile or acetone and obtained with the usual techniques of precipitation or crystallisation of the corresponding salts.

During any of the synthesis sequences described, or in the preparation of the sintones used it may be necessary and/or desirable to protect sensitive or reactive groups in some of the molecules employed. This can be performed by means of conventional protective groups such as those described in the literature [Protective

groups in Organic Chemistry, ed J. F.W. McOmie, Plenum Press, **1973**; T.W. Greene & P.G.M. Wuts, Protective Groups in Organic Chemistry, John Wiley & sons, **1991**]. The protective groups can be removed in a suitable latter stage by known methods.

The invention provides pharmaceutical compositions that comprise, in addition to an acceptable pharmaceutical excipient, at least one compound with the general formula (I) or one of its physiologically acceptable salts. The invention also relates to the use of a compound with the general formula (I) and its physiologically acceptable salts in the preparation of a medicament having serotonin $5HT_6$ receptor antagonistic activity, useful for preventing or treating various disorders of the Central Nervous System, and particularly anxiety, depression, cognitive memory disorders and senile dementia processes, and other dementias in which predominates a cognition deficit, psychosis, infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the serotonin 5-HT_6 receptor in mammals, including man.

The following examples show the preparation of novel compounds according to the invention. Also described is the affinity for the serotonin $5HT_6$ receptor, as well as galenic formulae applicable to the compounds object of the invention. The examples provided below are given for purposes of illustration only and should not restrict the scope of the invention in any way.

METHOD A

Example 7.- Preparation of N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-5-chloro-3-methyl-benzo[b]thiophene-2-sulphonamide.

To a solution of 3.05 g (15 mMol) of 5-amino-3-(2-dimethylaminoethyl)-1*H*-indole in 100 ml of pyridine is added dropwise at room temperature a solution of 4.21 g (15 mMol) of 5-chloro-3-methyl-benzo[b]thiophene-2-sulphonyl chloride in 20 ml of pyridine. The reaction mixture is stirred at room temperature for 20 hours. It is then evaporated to dryness, slightly alkalinised with diluted ammonia and dissolved in ethyl acetate. The organic phase is washed with water and a saturated solution of sodium bicarbonate, separated and dried with anhydrous sodium sulphate. The organic solution is evaporated to dryness and the resulting solid is repeatedly washed with ethyl ether, to yield 5.5 g (82%) of N-[3-(2-dimethylaminoethyl)-1*H*-indol-5-yl]-5-chloro-3-methyl-benzo[b]thiophene-2-sulphonamide as a solid with m.p.

= 226-227° C.

METHOD B

Example 26.- Preparation of N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-N-ethyl-naphthalene-2-sulphonamide.

To a mixture of 285 mg (0.7 mMol) of N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]naphthalene-2-sulphonamide (example 17) and 80 mg (0,7 mMol) of potassium t-butoxide in 3 ml of DMSO are stirred for 30 minutes at room temperature. Then 105 mg (0.7 mMol) of ethyl iodide are added and the solution is left with stirring for 3 hours. Water is added and the solution is extracted with ethyl acetate. The organic solution is evaporated to dryness and the resulting crude is purified by chromatography on silica gel, using as an eluent mixtures of methylene chloride/methanol/ammonia, yielding N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]-N-ethyl-naphthalene-2-sulphonamide as a solid with m.p. = 49-50° C.

METHOD C

Example 18.- Preparation of N-[3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide.

To a solution of 712 mg (13.2 mMol) of sodium methoxide in 100 ml of methanol, 850 mg (2.64 mMol) of N-[1*H*-indol-5-yl]naphthalene-1-sulphonamide are added, followed by 596 mg (5.28 mMol) of 1-methyl-4-piperidone and the resulting solution is heated to reflux for 48 hours. The reaction mixture is concentrated at reduced pressure and the residue obtained is purified by chromatography over silica gel, using as an eluent mixtures of methylene chloride/methanol/ammonia, to yield 573 mg (52%) of N-[3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide as a solid with m.p. = 244-245° C.

METHOD D

Example 12.- Preparation of N-[3-(1-methyl-piperidin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide.

To a solution of 417 mg (1 mMol) of N-[3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide in 50 ml of

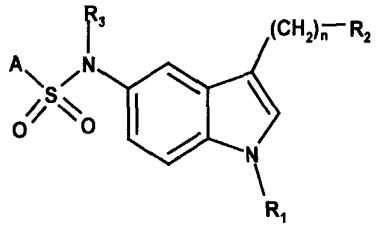
methanol, 100 mg of 5% palladium on carbon are added. The mixture is hydrogenated at room temperature at an initial hydrogen pressure of 3 atmospheres for 20 hours. The reaction mixture is filtered and the filtrate is concentrated at reduced pressure to provide a crude that is slurried in ethyl ether, yielding 272 mg (65%) of N-[3-(1-methyl-piperidin-4-yl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide as a solid with m.p.= 254-256° C

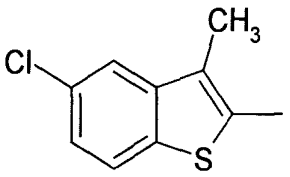
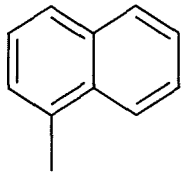
METHOD E

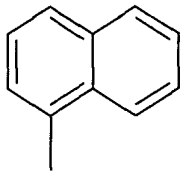
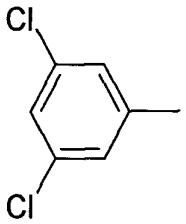
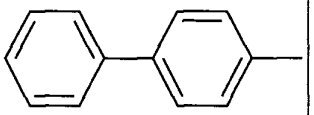
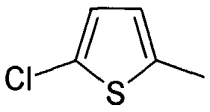
Example 3.- Preparation of N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide hydrochloride.

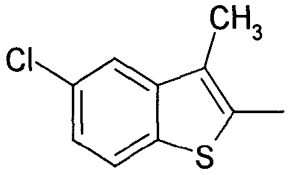
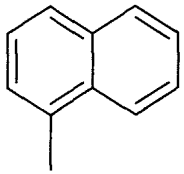
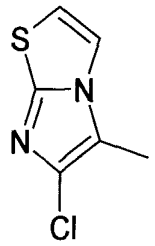
1.05 g (2.5 mMol) of N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide (example 2) are dissolved in 10 ml of ethanol, and 0.6 ml of a 4.2 N solution of hydrochloric acid in ethanol are added. It is allowed to crystallise at room temperature. N-[3-(2-diethylaminoethyl)-1*H*-indol-5-yl]naphthalene-1-sulphonamide hydrochloride is obtained as a solid with m.p.= 255-257° C.

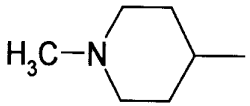
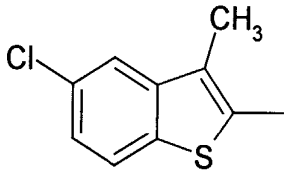
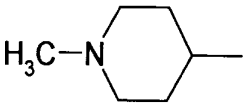
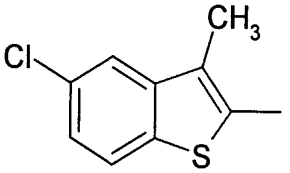
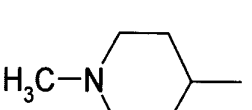
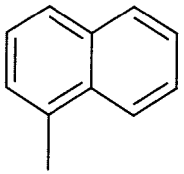
The melting point and spectroscopic data for identifying some of the compounds object of the present invention are shown in the following table:

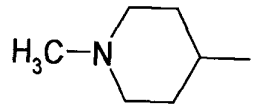
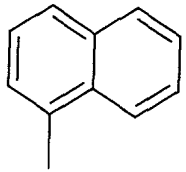
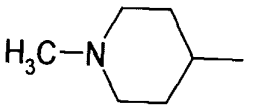
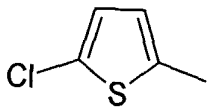
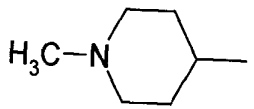
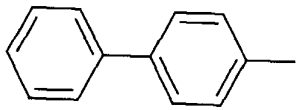


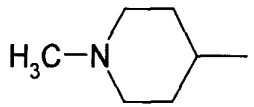
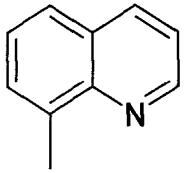
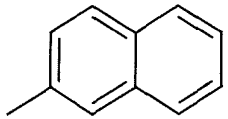
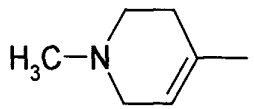
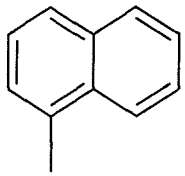
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
1	H	$(CH_3CH_2)_2N$-	2	H		–	170-173	3387, 2970, 2931, 1466, 1236, 1158, 1107, 1080, 993, 862, 805, 657, 565.	0.88(t, 6H, J=7.1 Hz); 2.28(s, 3H); 2.30-2.46(m, 6H); 2.58(m, 2H); 6.85(dd, 1H, J=8.6, 2.0 Hz); 7.10(m, 2H); 7.20(d, 1H, J=8.6 Hz); 7.50(dd, 1H, J=8.7, 2.0 Hz); 7.90(d, 1H, J=2.0 Hz); 7.98(d, 1H, J=8.7 Hz); 10.10 (bb 1H); 10.80(s, 1H). (DMSO-d6)
2	H	$(CH_3CH_2)_2N$-	2	H		–	170	3451, 3337, 2972, 1466, 1319, 1237, 1157, 1132, 1091, 991, 770, 675, 583, 481.	0.90(t, 6H, J=7.1 Hz); 2.33-2,55(m, 8H); 6.69(dd, 1H, J=8.7, 1.8 Hz); 6.95(s, 1H); 7.02(d, 1H, J=1,8 Hz); 7.05(d, 1H, J=8.7 Hz); 7.47(t, 1H, J=7.7 Hz); 7.63(m, 1H); 7.70(m, 1H); 8.01(m, 2H); 8.12(d, 1H, J=7.5 Hz); 8.77(d, 1H, J=8.1 Hz); 10.10(bb, 1H) 10,66(s, 1H) (DMSO-d6)

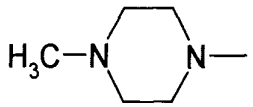
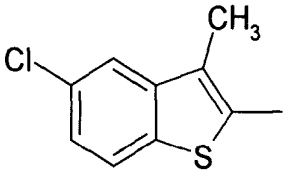
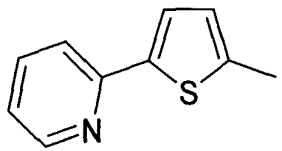
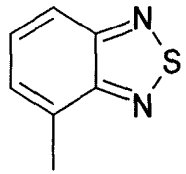
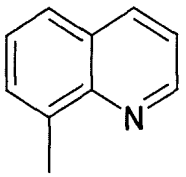
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
3	H	$(CH_3CH_2)_2N$-	2	H		HCl	255-257	3378, 3065, 2558, 2489, 1460, 1317, 1162, 1143, 1131, 811, 687, 602, 588.	1.22(t, 6H, J=7.2 Hz); 2.91-3.18(m, 8H); 6.65(d, 1H, J=8.6 Hz); 7.08(d, 1 J=8.6 Hz); 7.17(s, 1H); 7.20(d, 1H, J=1.8 Hz); 7.54(t, 1H, J=7.8 Hz); 7.63(m, 1H); 7.70(m, 1H); 8.03(d, 1H J=7.8 Hz); 8.08(d, 1H, J=7.1 Hz); 8.14(d, 1H, J=8.2 Hz); 8.79(d, 1H, J=8.4 Hz); 10.26(s, 1H); 10.90(bb, 1H); 11.01(s, 1H). (DMSO-d6)
4	H	$(CH_3CH_2)_2N$-	2	H		–	168-170	3309, 3047, 2974, 1566, 1467, 1235, 1167, 1143, 1116, 1001, 910, 799, 672, 587.	0.95(t, 6H, J=7.1 Hz); 2.44-2.58(m, 6H); 2.66(m, 2H); 6.79(dd, 1H, J=8.6 1.7 Hz); 7.08(d, 1H, J=0.9 Hz); 7.13(1H, J=1.7 Hz); 7.23(d, 1H, J=8.6 Hz) 7.58 (m, 2H); 7.87(m, 1H); 9,95(bb, 1H); 10.82(s, 1H). (DMSO-d6)
5	H	$(CH_3CH_2)_2N$-	2	H		–	161-163	3387, 2971, 1323, 1157, 1095, 765, 670, 590	0.89(t, 6H, J=7.1 Hz); 2.32-2.55(m, 6H); 2.62(m, 2H); 6.85(d, 1H, J=8.6 Hz); 7.08(d, 1H, J=2.0 Hz); 7.13(s, 1H); 7.18(d, 1H, J=8.6 Hz); 7.33-7.5((m, 3H); 7.64(d, 2H, J=7.5 Hz); 7.72(sys AB, 2H, J=8.6 Hz); 7,78(sys AB, 2H, J=8.6 Hz); 9.80(bb, 1H); 10.75(s, 1H). (DMSO-d6)
6	H	$(CH_3CH_2)_2N$-	2	H		–	180-181	3375, 2978, 1467, 1417, 1236, 1212, 1115, 994, 624.	0.96(t, 6H, J=7.1 Hz); 2.52(m, 4H); 2.57(m, 2H); 2.66(m, 2H); 6.83(dd, 1 J=8.6, 1.9 Hz); 7.11(d, 1H, J=4.0 Hz) 7.14(d, 1H, J=1.9 Hz); 7.17(d, 1H, J=1.9 Hz); 7.20-7.24(m, 2H); 10.01(b 1H); 10.81(s, 1H). (DMSO-d6)

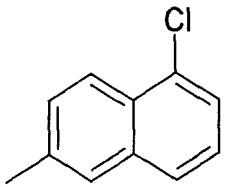
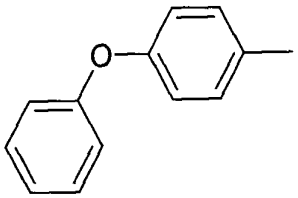
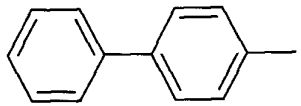
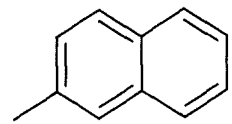
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
7	H	$(CH_3)_2N$-	2	H		–	226-227	3422, 3238, 1332, 1155, 1114, 1079, 986, 861, 803, 655, 564.	2.04(s, 6H); 2.23(m, 2H); 2.28(s, 3H) 2.59(m, 2H); 6.83(dd, 1H, J=8.4, 1.5 Hz); 7,09 (s, 2H); 7.19(d, 1H, J=8.4 Hz); 7.49(dd, 1H, J=8.7, 1.6 Hz); 7.91(d, 1H, J=1.6 Hz); 7.99(d, 1H, J=8.7 Hz); 10,13(bb, 1H), 10,79 (s, 1H) (DMSO-d6)
8	H	$(CH_3)_2N$-	2	H		–	203-205	3357, 1475, 1282, 1157, 1127, 990, 957, 809, 773, 613, 587, 557, 498.	2.09(s, 6H); 2.21(m, 2H); 2.54(m, 2H 6.69(dd, 1H, J=8.6, 1.7 Hz); 6,94 (s, 1H); 7.03 (s, 1H); 7.06(d, 1H, J=8.1 Hz); 7.49(t, 1H, J=7.8 Hz); 7.64(m, 1H); 7.71(m, 1H); 8.02 (m, 2H); 8.13(1H, J=8.1 Hz); 8.79(d, 1H, J=8.4 Hz) 10.10(bb, 1H); 10.68(s, 1H) (DMSO-d6)
9	H	$(CH_3)_2N$-	2	H		–	215 (dec)	3247, 3094, 1467, 1272, 1261, 1230, 625	2.17(s, 6 H); 2.36(m, 2 H); 2.65(m, 2 H); 6.77(dd, J=8.6, 1.7 Hz, 1 H); 7.07(1 H); 7.09(s, 1H); 7.18(d, J=8.6 Hz, 1 H); 7.51(d, J=4.5 Hz, 1 H); 7.81(d, J=4.5 Hz, 1 H); 10.80 (s, 1 H). (DMSC d6).

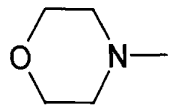
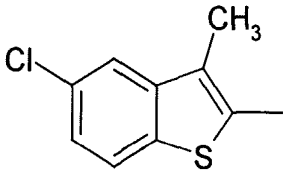
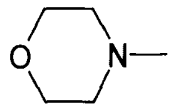
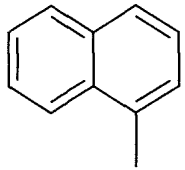
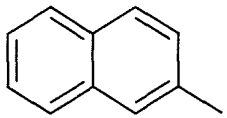
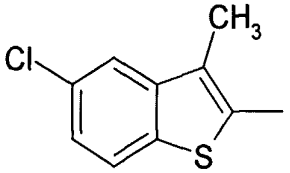
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
10	H		0	H		–	250 (dec)	3407, 2390, 1466, 1334, 1156, 113, 1080, 651, 565.	1.53-1.80(m, 4H); 2.26(s, 3H); 2.39-2.71(m, 6H); 3.02(d, 2H, J=8.8 Hz); 6.76(d, 1H, J=8.8 Hz); 7.05(s, 1H); 7.11(s, 1H); 7.19(d, 1H, J=8.8 Hz); 7.51(d, 1H, J=8.7 Hz); 7.91(s, 1H); 8.00(d, 1H, J=8.7 Hz); 10.10(bb, 1H) 10.90(s, 1H). (DMSO-d6)
11	H		0	H		HCl	220 (dec)	3423, 3214, 3043, 2942, 2688, 1464, 1317, 1149, 1114, 1080, 748, 670, 646	1.75-1.92(m, 4H); 2.31(s, 3H); 2.66(s 3H); 2.80(m, 1H); 2.95(m, 2H); 3.24(2H, J=11.4 Hz); 6.76(d, 1H, J=8.7 Hz 7.07(s, 1H); 7.19(m, 2H); 7.50(d, 1H, J=8.6 Hz); 7.93(s, 1Hz); 8.01(d, 1H, J=8.6 Hz); 8,34 (s, 1H); 10.90(bb, 1H 11.01(s, 1H). (DMSO-d6)
12	H		0	H		–	254-256	3343, 2938, 2929, 1470 1154, 1121, 1108, 988, 947, 805, 769, 589.	1.49(m, 2H); 1.61(m, 2H); 2.14(m, 2H 2.30(s, 3H); 2.40(m, 1H); 2,90 (d, 2H J=10.6 Hz) ; 6.65(d, 1H, J=8.6 Hz); 6.90(s, 1H); 6.96(s, 1H); 7.05(d, 1H, J=8.6Hz); 7.46(dt, 1H, J=7.51, 1.83 Hz); 7.64(m, 1H); 7.71(m, 1H); 7.99(1H, J=8.6 Hz); 8.03(d, 1H, J=8.6Hz); 8.12(d, 1H, J=8.2 Hz); 8.77(d, 1H, J=8.6 Hz); 10.07(bb, 1H); 10.71(s, 1H). (DMSO-d6)

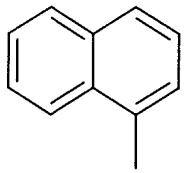
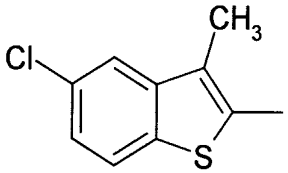
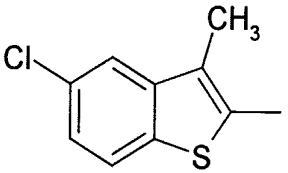
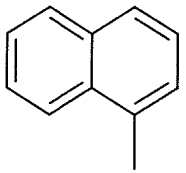
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
13	H		0	H		HCl	212 (dec)	3423, 3269, 3114, 2955, 2733, 1469, 1321,1155, 1133, 947, 769.	1.80(m, 4H); 2.74(m, 4H); 3.04(m, 2H 3.39(m, 2H); 6.63(d, 1H, J=8.6 Hz); 7.00(s, 2H); 7.08(d, 1H, J=8.6 Hz);7.49(t, 1H, J=7.7 Hz); 7.60-7.77(m, 2H); 8.04(d, 2H, J=7.5 Hz); 8.13(d, 1H, J=8.2 Hz); 8.79(d, 1H, J=8.2 Hz); 10.16(s, 1H); 10.66(bb, 1H); 10.88(s, 1H). (DMSO-d6)
14	H		0	H		–	284 (dec)	3371, 2943, 1468, 1410, 1324, 1148, 993, 604.	1.62(m, 2H); 1.78(d, 2H, J=11.7 Hz); 1.99(m, 2H); 2.18(s, 3H); 2.55(m, 1H 2.84(d, 2H, J=10.6 Hz); 6.81(d, 1H, J=8.6 Hz); 7.07(s, 1H); 7.13(m 1H); 7.16(s, 1H); 7.20-7.26 (m, 1H); 9.90 (bb, 1H); 10.83 (s, 1H). (DMSO-d6)
15	H		0	H		–	247-248	3361, 2936, 1318, 1155, 1095, 767, 670, 587.	1.52(s, 2H); 1.67(m, 2H); 1.85(m, 2H 2.08(s, 3H); 2.44(m, 1H); 2.67(d, 2H, 10.25Hz); 6.83(d, 1H, J=8.4 Hz); 7.01(s, 1H); 7,03(s, 1H); 7.19(d, 1H, J=8.4 Hz); 7.35-7.50(m, 3H); 7.63-7.73(m, 4H); 7.79(sys AB, 2H, J=7.6 Hz); 9.71(bb, 1H); 10.76(s, 1H) (DMSO-d6).

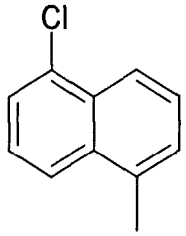
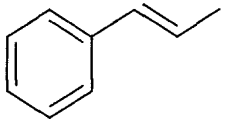
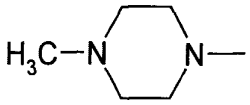
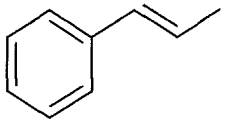
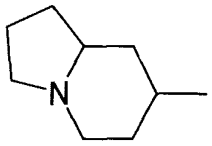
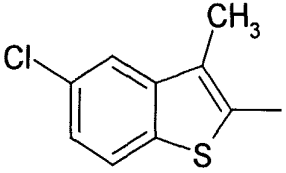
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
16	H		0	H		–	280 (dec)	3398, 3257, 2933, 1161, 1143, 789, 589.	1.25-1.52(m, 4 H); 1.85(m, 2 H); 2.18(3 H); 2.27(m, 1 H); 2.74 (d, J=11.4 Hz 2 H); 6.72(dd, J=8.6, 2.0 Hz, 1 H); 6.83(d, J=1.5 Hz, 1 H); 6.90(d, J=2.0 Hz, 1 H); 7.02(d, J=8.6 Hz, 1 H); 7.57(m, 1 H); 7.74(dd, J=8.4, 4.3 Hz, H); 8.12 (dd, J=7.3, 1.3 Hz, 1 H); 8.19(dd, J=8.2, 1.3 Hz, 1 H); 8.52(dd, J=8.4, 1.7 Hz, 1 H); 9.21(dd, J=4.3, 1. Hz, 1 H); 9.36(s, 1 H); 10.64(s, 1 H). (DMSO-d6).
17	H	$(CH_3CH_2)_2N$-	2	H		–	172-173	3199, 2970, 2930, 2870, 1327, 1153, 1130, 1110, 1075, 956, 676, 658, 551, 476.	0.87(t, J=7.1 Hz, 6 H); 2.39(m, 6 H); 2.55 (m, 2 H);); 6.82(d, J=8.6 Hz, 1 H 7.05 (s, 1 H); 7.09(s, 1 H); 7.13(d, J=8.6 Hz, 1 H); 7.60(m, 2 H); 7.73 (d, J=8.6 Hz, 1 H); 7.95(d, J=7.9 Hz, 1 H 8.01 (m, 2 H); 8.26 (s, 1 H); 9.86(bb, H); 10.71(s, 1 H). (DMSO-d6).
18	H		0	H		–	244-245 (dec)	3346, 2943, 1474, 1283, 1261, 1156, 1123, 801, 771, 589, 503.	2.25(s, 3 H); 2.31(m, 2 H); 2.46(m, 2 H); 2.90(m, 2 H); 5.34(s, 1 H); 6.78(d J=8.6, 2.0 Hz, 1 H); 7.09(d, J=1.5 Hz, H); 7.14 (d, J=8.6 Hz, 1 H); 7.25 (d, J=2.0 Hz, 1 H); 7.49(t, J=7.8 Hz, 1 H) 7.66(m, 1 H); 7.75(m, 1 H); 8.04(m, 2H); 8.14(d, J=8.2 Hz, 1 H); 8.83(d, J=8.6 Hz, 1 H); 10.14(bb, 1 H); 11.03(1 H). (DMSO-d6).

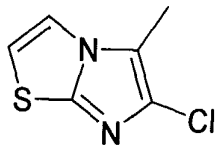
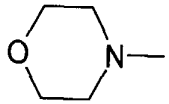
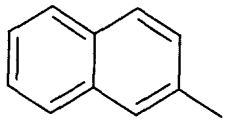
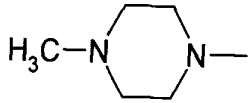
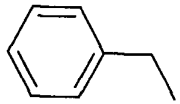
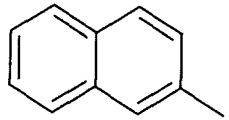
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
19	H		1	H		–	230 (dec)	2796, 1452, 1316, 1149, 1114, 1080, 1001, 810, 646, 559.	1.80-2.26(m, 8 H); 2.04(s, 3 H); 2.30(s 3 H); 3.41(s, 2 H); 6.89(dd, J=8.6, 1.5 Hz, 1 H); 7.16(s, 1 H); 7.22(d, J=8.6 H 1 H); 7.29(s, 1 H); 7.49(dd, J=8.7, 1.7 Hz, 1 H); 7.90(d, J=1.7 Hz, 1 H); 7.98(d, J=8.7 Hz, 1 H); 10.13(bb, 1 H) 10.93(s, 1 H). (DMSO-d6).
20	H	$(CH_3)_2N$-	2	H		–	209-211	3377, 2951,2798, 1469, 1429, 1321, 1158, 777, 594.	2.05(s, 6 H); 2.32(m, 2 H); 2.65(m, 2 H); 6.86(dd, J=8.6, 1.8 Hz, 1 H); 7.10(J=1.8 Hz, 1 H); 7.18(d, J=1.8 Hz, 1 H 7.21 (d, J=8.6 Hz, 1 H); 7.32(dd, J=7. 4.6 Hz, 1 H); 7.36(d, J=3.9 Hz, 1 H); 7.71(d, J=3.9 Hz, 1 H); 7.83(m, 1 H); 7.93(m, 1 H); 8.49(d, J=4.6 Hz, 1 H); 9.97(bb, 1 H); 10.79(s, 1 H). (DMSO-d6).
21	H	$(CH_3)_2N$-	2	H		–	192	3321, 2949, 1474, 1327, 1152, 1138, 1104, 981, 614.	2.10(s, 6 H); 2.21(m, 2 H); 2.56(m, 2 H); 6.72(d, J=8.6 Hz, 1 H); 6.96(s, 1 H 7.03 (s, 1 H); 7.07(d, J=8.6 Hz, 1 H); 7.70(m, 1 H); 8.07(d, J=7.0 Hz, 1 H); 8.29(d, J=8.8 Hz, 1 H); 10.14(bb, 1 H) 10.69(s, 1 H). (DMSO-d6).
22	H	$(CH_3)_2N$-	2	H		–	250 (dec)	3252, 2857, 1459, 1426, 1333, 1161, 1144, 789, 680, 589.	2.07(s, 6 H); 2.16(m, 2 H); 2.51(m, 2 H); 6.73(dd, J=8.6, 1.8 Hz, 1 H); 6.94(1 H) 6.99(s, 1 H); 7.02(d, J=8.6 Hz, 1 H); 7.59(t, J=7.8 Hz, 1 H); 7.73(dd, J=8.4, 4.1 Hz, 1 H); 8.18(m, 2 H); 8.50(dd, J=8.4, 1.5 Hz, 1 H); 9.20(dd, J=4.1, 1.5 Hz, 1 H); 9.45(bb, 1 H); 10.64(s, 1 H). (DMSO-d6).

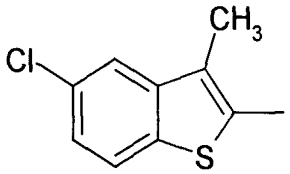
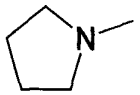
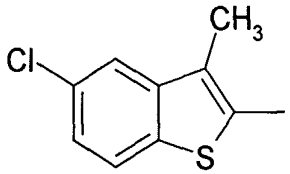
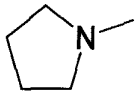
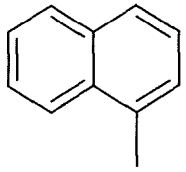
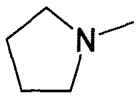
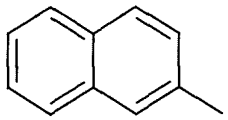
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
23	H	$(CH_3)_2N$-	2	H		–	230-240 (dec)	3404, 2944, 2918,2855, 1465, 1332, 1157, 1140, 1080, 650, 639, 526.	2.01(s, 6 H); 2.18(m, 2 H); 2.57(m, 2 H); 6.81 (dd, J=8.6, 1.7 Hz, 1 H); 7.02 (s, 1 H); 7.05(d, J=1.7 Hz, 1 H); 7.15(J=8.6 Hz, 1 H); 7.57(m, 1 H); 7.82(d, J=7.5 Hz, 1 H); 7.91(d, J=8.9 Hz, 1 H 8.06(d, J=8.2 Hz, 1 H); 8.29(d, J=8.9 Hz, 1 H); 8.35(s, 1 H); 9.94(bb, 1 H); 10.74(s, 1 H). (DMSO-d6).
24	H	$(CH_3)_2N$-	2	H		–	152-154	3232, 2862, 2827, 2785, 1583, 1488, 1333, 1248, 1155, 1091, 755, 693, 571, 541.	2.16(s, 6 H); 2.37(m, 2 H); 2.66 (m, 2 H); 6.80 (d, J=8.6 Hz, 1 H); 6.96-7.12 (m, 6 H); 7.14-7.25 (m, 2 H); 7.41(m, 2 H); 7.64 (dd, J=8.5, 1.9 Hz, H); 9.69(bb, 1 H); 10.75 (s, 1 H). (DMSO-d6).
25	H	$(CH_3)_2N$-	2	H		–	184-186	3451, 3388, 2950, 2775, 1466, 1322, 1159, 1095, 763, 670, 591.	2.08(s, 6 H); 2.32(m, 2 H); 2.64(m, 2 H); 6.83(dd, J=8.6, 1.9 Hz, 1 H); 7.08(J=2.0 Hz, 1 H); 7.11(d, J=1.9 Hz, 1 H 7.17(d, J=8.6 Hz, 1 H); 7.34-7.50(m, 3H); 7.66(d, J=7.5 Hz, 2 H); 7.72(AB sys, J=8.6 Hz, 2 H); 7.79(AB sys, J=8 Hz, 2 H); 9.79(s, 1 H); 10.75(s, 1 H). (DMSO-d6).
26	H	$(CH_3CH_2)_2N$-	2	Et		–	49-50	3386, 2970, 2931, 1474, 1337, 1167, 1151, 1130, 1073, 661,550	0.82(t, J=7.0 Hz, 6 H); 0.98(t, J=7.0 H 3 H); 2.37(q, J=7.0 Hz, 4 H); 2.49(m, H); 2.54(m, 2H); 3.66(q, J=7.1 Hz, 2 H 6.73 (dd, J=8.61, 1.6 Hz, 1 H); 6.98(s H); 7.17 (d, J=1.6 Hz, 1 H); 7.26(d, J=8.61 Hz, 1 H); 7.56-7.72 (m, 3 H); 7.99-8.11(m, 3H); 8.26 (s, 1 H); 10.97(s, 1 H). (DMSO-d6).

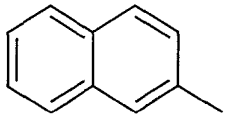
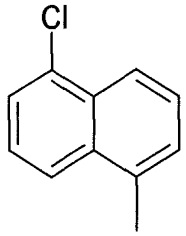
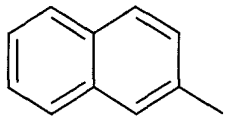
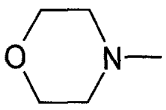
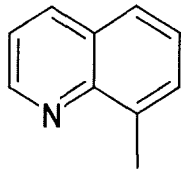
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
27	H		2	H		–	200-201	3366, 2951, 2816, 1460, 1421, 1319, 1283, 1157, 1114, 1078, 865, 651, 561	2.25(m, 6H); 2.27(s, 3H); 2.62(t, J=7. Hz, 2H); 3.52(m, 4H); 6.84(d, J=8.2 Hz, 1H); 7.06(s, 1H); 7.10(s, 1H); 7.20(d, J=8.6 Hz, 1H); 7.50(d, J=8.6 Hz, 1H); 7.92(s, 1H); 8.00 (d, J=8.6 Hz, 1H); 10.13(s, 1H); 10.80(s, 1H). (DMSO-d6)
28	H		2	H		–	218-220	3389, 3152, 2916, 2819, 1466, 1313, 1157, 1129, 1108, 771, 587	2.30(m, 6H); 2.56(m, 2H); 3.56(m, 4H 6.69(d, J=8.4 Hz, 1H); 6.93(s, 1H); 7.06(m, 2H); 7.48(t, J=7.3 Hz, 1H); 7.67(m, 2H); 8.02(m, 2H); 8.13 (d, J=8.1 Hz, 1H); 8.78 (d, J=8.1 Hz, 1H 10.10(s, 1H); 10.68(s, 1H). (DMSO-d
29	H	$(CH_3CH_2)_2N$-	2	CH_3		–	134-136	2968, 2930, 1488, 1329, 1159, 1131, 1074, 660, 550	0.98(t, J=7.1 Hz, 6H); 2.55(m, 6H); 2.70(m, 2H); 3.67(s, 3H); 6.84 (s. 1H 6.93(dd, J=8.6, 2 Hz, 1H); 7.10(d, J=8.7 Hz, 1H); 7.18(d, J=1.7 Hz, 1H) 7.26(s, 1H); 7.57 (m, 2H); 7.67(dd, J=8.7, 1.8 Hz, 1H); 7.84(m, 3H); 8.27(d, J= 1.7 Hz, 1H). (DMSO-d6)
30	H	$(CH_3)_2N$-	1	H		–	148-152	3398, 2930, 1467, 1158, 1113, 1079, 861, 803, 651, 561	1.89(m, 6H); 2.29(s, 3H); 2.48(s, 2H) 6.83(m, 1H); 7.18(m, 3H); 7.50(m, 1H 7.91(m, 1H); 8.00 (m, 1H); 10.13(b, 1H); 10.92(s, 1H). (DMSO-d6)

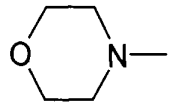
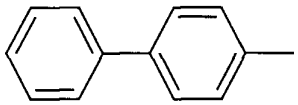
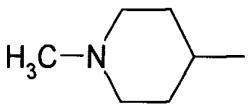
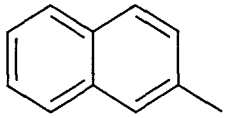
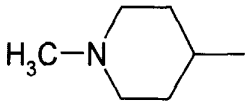
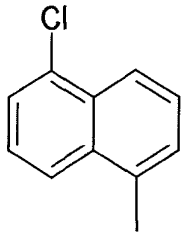
Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
31	H	$(CH_3CH_2CH_2)_2N$-	2	H		–	76-80	3399, 2959, 2931, 1466, 1159, 1132, 802, 770, 588	0.82(t, J=6.7 Hz, 6H); 1.34(q, J=6,71 Hz, 4H); 2.31(m, 4H); 2.40(m, 2H); 2.52(m, 2H); 6.69(d, J=8.6 Hz, 1H); 7.04(m, 3H); 7.47(m, 1H); 7.66(m, 2H 8.02(m, 2H); 8.11(d, J=8.1 Hz, 1H); 8.78(d, J=8.4 Hz, 1H); 10.12(s, 1H); 10.67(s, 1H). (DMSO-d6)
32	H	$(CH_3CH_2CH_2)_2N$-	2	H		–	90-95	3406, 2959, 2932, 2872, 1466, 1157, 1079, 861, 652, 561	0.80(t, J=7.3 Hz, 6H); 1.31(q, J=7.3 Hz, 4H); 2.26(m, 7H); 2.38(m, 2H); 2.56(m, 2H); 6.83(dd, J=8.4, 1.8 Hz, 1H); 7.08(s, 2H); 7.20(d, J=8.6 Hz, 1H); 7.50(dd, J=8.6, 2.0 Hz, 1H); 7.90(d, J=2.0 Hz, 1H); 7.99(d, J=8.6 Hz, 1H); 10.12(b, 1H); 10.79(s, 1H). (DMSO-d6)
33	H	$(CH_3CH_2CH_2CH_2)_2N$-	2	H		–	79-80	3398, 2956, 2930, 2870, 1466, 1158, 1080, 862, 801, 653, 562	0.84(t, J=6.8 Hz, 6H); 1.24(m, 8H); 2.26(s, 3H); 2.28(m, 4H); 2.39(m, 2H 2.57(m, 2H); 6.82(dd, J=8.6, 1.9 Hz, 1H); 7.09(d, J=1.8 Hz, 2H); 7.18(d, J=8.6 Hz, 1H); 7.50(dd, J=8.6, 1.9 Hz 1H); 7.89(d, J=1.8 Hz, 1H); 7.98(d, J=8.6 Hz, 1H); 10.14(b, 1H); 10.78(s 1H). (DMSO-d6)
34	H	$(CH_3CH_2CH_2CH_2)_2N$-	2	H		–	111-113	3291, 2955, 2926, 2870, 1327, 1158, 1136, 772, 676, 611, 585	0.86(t, J=7.0 Hz, 6H); 1.29(m, 8H); 2.35(m, 4H); 2.41(m, 2H); 2.53(m, 2H 6.67(dd, J=8.5, 1.9 Hz, 1H); 7.09(m, 3H); 7.48(t, J=7.9 Hz, 1H); 7.68(m, 2H); 8.01(s, , 1H); 8.04(s, 1H); 8.12(d J=8.2 Hz, 1H); 8.78(d, J=8.2 Hz, 1H) 10.13(s, 1H); 10.67(s, 1H). (DMSO-d

Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
35	H	$(CH_3CH_2)_2N$-	2	H		–	154-156	3402, 2978, 1471, 1285, 1162, 1135, 1018, 780, 629, 606	0.88(t, J=6.7 Hz, 6H); 2.41(m, 6H); 2.49(m, 2H); 6.71(d, J=8.1 Hz, 1H); 6.88(s, 1H); 7.07(m, 2H); 7.66(m, 2H 7.84(d, J=7.0 Hz, 1H); 8.09(d, J=7.0 Hz, 1H); 8.41(d, J=8.2 Hz, 1H); 8.79(J=8.6 Hz, 1H); 10.17(b, 1H); 10.71(s 1H). (DMSO-d6)
36	H	$(CH_3CH_2)_2N$-	2	H		–	125-130	3404, 2972, 1473, 1319, 1142, 967, 745, 541	0.94(t, J=7.1 Hz, 6H); 2.50(q, J=7.1 Hz, 4H); 2.59(m, 2H); 2.68(m, 2H); 6.94(dd, J=8.6, 1.8 Hz, 1H); 7.26(m, 8H); 7.59(m, 2H); 9.54(b, 1H); 10.77(1H). (DMSO-d6)
37	H		1	H		–	203 (dec)	2809, 1340, 1150, 746, 542	2.06(s, 3H); 2.22(m, 6H); 3.36(m 2H) 3.49 (s, 2H); 6.95(dd, J=8.6, 1.8 Hz, 1H); 7.18(s, 2H); 7.24(m, 2H); 7.37(n 3H); 7.45(d, J=1.8 Hz, 1H); 7.61(m, 2H); 9.53(s 1H); 10.90(s, 1H). (DMS(d6)
38	H		0	H		–	142-144	3413, 2929, 1157, 1113, 1080, 862, 651, 564	1.12(m, 3H); 1.81(m, 9H); 2.22(s, 3H 2.93(m, 2H); 6.84(dd, J=8.5, 1.7 Hz, 1H); 6.99(s, 1H); 7.03(s, 1H); 7,20(d, J=8.6 Hz, 1H); 7.52(dd, J=8.6, 2.0 H: 1H); 7.90(d, J=1.7 Hz, 1H); 8.00(d, J=8.6 Hz, 1H); 10.01(b, 1H); 10.61(s 1H). (DMSO-d6)

Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
39	H	$(CH_3CH_2)_2N$-	2	H		–	197-198	3338, 1466, 1270, 1237, 117, 986, 626	0.96(t, J=7.1 Hz, 6H); 2.53(m, 6H); 2.63(m, 2H); 6.78(dd, J=8.5, 1.6 Hz, 1H); 7.10(s, 2H); 7.18(d, J=8.6 Hz, 1H); 7.51(d, J=4.6 Hz, 1H); 7.80(d, J=4.6 Hz, 1H); 10.78(s, 1H). (DMSO-d6)
40	H		2	H		–	85-90	3399, 3257, 2920, 2855, 2814, 1460, 1330, 1157, 1131, 1113, 1074, 659, 551, 477	2.27(m, 6H); 2.61(t, J=7.9 Hz, 2H); 3.52(t, J=4.6 Hz, 4H); 6.82(dd, J=8.6 2.0 Hz, 1H); 7.06(s, 1H); 7.07(s, 1H); 7.15(d, J=8.6 Hz, 1H); 7.61(m, 2H); 7.74(dd, J=8.8, 1.8 Hz, 1H); 7.96(d, J=8.1 Hz, 1H); 8.03(m, 2H); 8.27 (s, 1H); 9.87(s, 1H); 10.74(s, 1H). (DMSO-d6)
41	H		1	H		–	99-102	3398, 2934, 2806, 1458, 1331, 1284, 1153, 1127, 700, 542	2.11(s, 3H); 2.32(m, 6H); 3.35(m, 2H 3.56(s, 2H); 4.29(s, 2H); 6.98(d, J=8. Hz, 1H); 7.29(m, 7H); 7.53(s, 1H); 9.40(s, 1H); 10.94(s, 1H). (DMSO-d6
42	H	$(CH_3CH_2)_2N$-	3	H		–	128-130	3259, 2973, 2939, 2827, 1468, 1332, 1159, 1131, 1075, 670, 555	0.86(t, J=7.0 Hz, 6H); 1.51(t, J=6.9 H 2H); 2.27(t, J=6.9 Hz, 2H); 2.35(q, J=7.0 Hz, 4H); 2.46(m, 2H); 6.77(d, J=8.6Hz, 1H); 7.00(s, 1H); 7.10(m, 2H); 7.60(m, 2H); 7.72(d, J=8.8 Hz, 1H); 7.95(d, J=7.9 Hz, 1H); 8.02(m, 2H); 8.26(s, 1H); 9.86 (b, 1H); 10.67(1H). (DMSO-d6)

Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
43	H	$(CH_3CH_2)_2N$-	3	H		–	156-158	3247, 2969, 2938, 1467, 1340, 1159, 1113, 1080, 862, 666, 558	0.88(t, J=7.0 Hz, 6H); 1.52(m, 2H); 2.29(m, 5H); 2,37(q, J=7.0 Hz, 4H); 2.47(m, 2H); 6.81(dd, J=8.6, 1.5 Hz, 1H); 7.06(d, J=1.6 Hz, 1H); 7.12(d, J=1.5 Hz, 1H); 7.18(d, J=8.6 Hz, 1H) 7.51(dd, J=8.6, 2.0 Hz, 1H);); 7.91(d J=2.0 Hz, 1H); 7.99(d, J=8.6 Hz, 1H);10.06(b, 1H); 10.76(s, 1H). (DMSO-d6)
44	H		2	H		–	201-203	3386, 2929, 1466, 1157, 1106, 1080, 992, 861, 650, 564	1.62(m, 4H); 2.29(s, 3H); 2.30(m, 4H) 2.36(m, 2H); 2.63(m, 2H); 6.86(d, J=8 Hz, 1H); 7.05(s, 1H); 7.09(s, 1H); 7.21(dd, J=8.6, 2.2 Hz, 1H); 7.50(dd, J=8.7, 2.0 Hz, 1H); 7.92(s, 1H); 7.99(dd, J=8.7, 2.2 Hz, 1H); 10,10(b, 1H); 10.81(s, 1H). (DMSO-d6)
45	H		2	H		–	212-214	3354, 2964, 2812, 1466, 1201, 1157, 1124, 808, 773, 593	1.66(m, 4H); 2.36(m, 6H); 2.58(m, 2H 6.71(d, J=8.6 Hz, 1H); 6.93(s, 1H); 7.02(s, 1H); 7.07(d, J=8.6 Hz, 1H); 7.48 (m, 1H); 7,68(m, 2H); 8.02(dd, J=7.2, 1.2 Hz, 2H); 8.12(d, J=8.2 Hz, 1H); 8.79(d, J=8.6 Hz, 1H); 10.10(b, 1H); 10.68(s, 1H). (DMSO-d6)
46	H		2	H		–	180-182	3375, 2968, 2821, 1467, 1323, 1313, 1146,1139,113, 1079, 972, 654, 549	1.60(m, 4H); 2.26(m, 4H); 2.35(m, 2H 2.61(m, 2H); 6.82(dd, J=8.6, 2.0 Hz, 1H); 7.05(m, 2H); 7.14(d, J=8.6 Hz, 1H); 7.61(m, 2H); 7.74(dd, J=8.6, 1.8 Hz, 1H); 7.95(d, J=7.9 Hz, 1H); 8.02(m, 2H); 8.27(s, 1H); 9.86(b, 1H) 10.72(s, 1H). (DMSO-d6)

Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
47	H	$(CH_3CH_2CH_2)_2N$-	2	H		–	58-64 (dec)	3398, 3255, 2958, 2931, 2872, 1466, 1330, 1156, 1130, 1074, 659, 551	0.79(t, J=7.3 Hz, 6H); 1.31(q, J=7.3 Hz, 4H); 2.28(t, J=7.3 Hz, 4H); 2.42(t 2H); 2.57(m, 2H); 6.80(dd, J=8.6, 1.7 Hz, 1H); 7.04(d, J=1.7 Hz, 1H); 7.12(2H); 7.60(m, 2H); 7.72(dd, J=8.6, 1.7 Hz, 1H); 7.98(m, 3H); 8.25(s, 1H); 9.87(b, 1H); 10.70(s, 1H). (DMSO-d6
48	H	$(CH_3)_2N$-	2	H		–	201-203	3369, 1473, 1161, 1125, 1017, 789, 619	2.06(s, 6H); 2.15(t, J=8.2 Hz, 2H); 2.52(t, J=8.2 Hz, 2H); 6.69(d, J=8.7 Hz, 1H); 6.85(s, 1H); 7.02(s, 1H); 7.08(d, J=8.7 Hz, 1H); 7.67(m, 2H); 7.84(d, J=7.3 Hz, 1H); 8.10(d, J=7.3 Hz, 1H); 8.41(d, J=8.4 Hz, 1H); 8.79(J=8.7 Hz, 1H); 10.15(b, 1H); 10.70(s 1H). (DMSO-d6)
49	H	$(CH_3)_2N$-	2	H		–	180-190	3399, 3255, 2943, 1466, 1330, 1156, 1131, 1075, 659, 550	2.03(s, 6H); 2.22(t, J=8.2 Hz, 2H); 2.58(t, J=8.2 Hz, 2H); 6.80(d, J=8.4 Hz, 1H); 7.04(s, 1H); 7.07(s, 1H); 7.13(d, J=8.6 Hz, 1H); 7.60(m, 2H); 7.74(d, J=8.6 Hz, 1H); 7.95(d, J=7.7 Hz, 1H); 8.02(m, 2H); 8.26(s, 1H); 9.86(b, 1H); 10.71(s, 1H). (DMSO-d6
50	H		2	H		–	234-235	3400, 3279, 2913, 2852, 1464, 1420, 1315, 1163, 1118, 951, 592	2.29(m, 6H); 2.54(m, 2H); 3.57(m, 4H 6.72(d, J=8.1 Hz, 1H); 7.01(m, 3H); 7.60(t, J=7.7 Hz, 1H); 7.74(d, J=8.4 Hz, 1H); 8.19(m, 2H); 8.52(d, J=8.4 Hz, 1H); 9.21(s, 1H); 9.44(s, 1H); 10.65(s, 1H). (DMSO-d6)

Ex	R_1	R_2	n	R_3	A	Salt	m.p. ° C	IR cm^{-1}	^{1}H-NMR (300 MHz),δ (solvent)
51	H		2	H		–	225-228	3340, 2857, 1479, 1324, 1153, 1116, 1094, 768, 670, 588	2.29(m, 6H); 2.66(m, 2H); 3.47(m, 4H 6.84(d, J=8.6 Hz, 1H); 7.07(s, 1H); 7.09(s, 1H); 7.18(d, J=8.4 Hz, 1H); 7.45(m, 3H); 7.70(m, 4H); 7.79(m, 2H 9.79(s, 1H); 10.77(s, 1H). (DMSO-d6
52	H		2	H		–	129-131	3367, 2924, 2852, 2799, 1465, 1311, 1154, 1130, 1077, 666, 557	1.40-1.60(m, 4H); 1.83(m, 2H); 2.14(3H); 2.36(m, 1H); 2.67(d, J=11.2 Hz, 2H); 6 .78(d, J=8.4 Hz, 1H); 6.97(s, 1H); 7.00(s, 1H); 7.12(d, J=8.6 Hz, 1H); 7.50-7.68(m, 2H); 7.73(d, J=9.0 Hz, 1H); 8.00(m, 3H); 8.23(s, 1H); 9.78(b, 1H); 10.71(s, 1H). (DMSO-d6
53	H		2	H		–	246-249	3329, 2940, 2916, 1470, 1158, 1125, 1110, 1015, 791, 598	1.35-1.47(m, 4H); 1.86(m, 2H); 2.17(3H); 2.28(m, 1H); 2.76(d, J=10.6 Hz, 2H); 6 .68(d, J=8.8 Hz, 1H); 6.75(s, 1H); 6.94(s, 1H); 7.08(d, J=9.0 Hz, 1H); 7.60-7.73(m, 2H); 7.85(d, J=7.1 Hz, 1H); 8.06(d, J=7.1 Hz, 1H); 8.40(J=7.9 Hz, 1H); 8.79(d, J=9.0 Hz, 1H) 10.20(b, 1H); 10.68(s, 1H). (DMSO-d6)

BIOLOGICAL ASSAYS

BINDING TO SEROTONIN RECEPTOR $5HT_6$

Cell membranes of HEK-293 cells expressing the recombinant human $5HT_6$ receptor were supplied by Receptor Biology. In said membranes the receptor concentration is 2.18 pmol/mg protein and the protein concentration is 9.17 mg/ml. The experimental protocol follows the method of B. L. Roth et al. [B. L. Roth, S. C. Craigo, M. S. Choudhary, A. Uluer, F. J. Monsma, Y. Shen, H. Y. Meltzer, D. R. Sibley: Binding of Typical and Atypical Antipsychotic Agents to 5-Hydroxytryptamine-6 and Hydroxytriptamine-7 Receptors. *The Journal of Pharmacology and Experimental Therapeutics*, **1994**, *268*, 1403] with slight changes. The commercial membrane is diluted (1:40 dilution) with the binding buffer: 50 mM Tris-HCl, 10 mM $MgCl_2$, 0.5 mM EDTA (pH 7.4). The radioligand used is [^{3}H]-LSD at a concentration of 2.7 nM with a final volume of 200 µl. incubation is initiated by adding 100 µl of membrane suspension, (≈ 22.9 µg membrane protein), and is prolonged for 60 minutes at a temperature of 37° C. The incubation is ended by fast filtration in a Brandel Cell Harvester through fiber glass filters made by Schleicher & Schuell GF 3362 pretreated with a solution of polyethylenimine at 0.5 %. The filters are washed three times with three milliliters of buffer Tris-HCl 50 mM pH 7.4. The filters are transferred to flasks and 5 ml of Ecoscint H liquid scintillation cocktail are added to each flask. The flasks are allowed to reach equilibrium for several hours before counting with a Wallac Winspectral 1414 scintillation counter. Non-specific binding is determined in the presence of 100 µM of serotonin. Tests were made in triplicate. The inhibition constants (K_i, nM) were calculated by non-linear regression analysis using the program EBDA/LIGAND [Munson and Rodbard, *Analytical Biochemistry*, **1980**, *107*, 220]. The following table shows binding results for some of the compounds object of the present invention.

Table

Example	% Inhibition 10^{-6} M	K_i (nM)
1	98.1 ± 4.0	0.28
3	96.6 ± 5.2	3.5
4	96.2 ± 0.6	9.3
5	101.2 ± 0.1	1.0
6	97.6 ± 1.8	8.7
7	103.0 ± 7.9	0.13
8	94.5 ± 7.0	0.76
9	96.8 ± 3.7	2.2
11	101.3	0.98
13	98.3	4.7
14	95.7 ± 3.4	24.3
15	97.4 ± 0.8	6.8
16	94.4 ± 8.6	21.2
17	102.0	5.3

The daily posology in human medicine are between 1 milligram and 500 milligrams of product, which can be given in one or more administrations. The compositions are prepared in forms compatible with the route of administration used, such as tablets, sugar-coated pills, capsules, suppositories, solutions or suspensions. These compositions are prepared by known methods and comprise between 1 and 60% by weight of the active ingredient (compound with the general formula I) and 40 to 99% by weight of a suitable pharmaceutical excipient compatible with the active ingredient and the physical form of the composition used. By way of example, the formula of a tablet containing a product of the invention is shown.

Example of formula per tablet:

Example 1	5 mg
Lactose	60 mg
Crystalline cellulose	25 mg

K 90 Povidone	5 mg
Pregelatinised starch	3 mg
Colloidal silicon dioxide	1 mg
Magnesium stearate	1 mg
Total weight per tablet	100 mg